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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,400	11/29/2001	Chulso Moon	P-CAN 1004	4431
22907 7590 12/31/2007 BANNER & WITCOFF, LTD. 1100 13th STREET, N.W. SUITE 1200 WASHINGTON, DC 20005-4051			EXAMINER YU, MISOOK	
			ART UNIT 1642	PAPER NUMBER
			MAIL DATE 12/31/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<p align="center"><b>Office Action Summary</b></p>	<b>Application No.</b> 10/045,400	<b>Applicant(s)</b> MOON ET AL.	
	<b>Examiner</b> MISOOK YU	<b>Art Unit</b> 1642	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 45-48, 50-54, 56 and 58-66 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 45-48, 50-54, 56, and 58-66 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

Claims 1, 45-48, 50-54, 56, and 58-66 are pending and under consideration.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 53, 54, 56, and 58-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inbal et al., 1997, Nature 390:180-184 in view of Esteller et al., of record (1999, IDS, pages 67-70).

Claims 52, 53, 54, 56, and 58-66 are drawn to method of assessing aggressiveness of a NSCLC tumor in a human comprising assessing expression of the gene encoding DAP-kinase in lung cells of the human, whereby a lower degree of expression of the gene is an indication that the tumor is aggressive, wherein a more aggressive treatment is selected when lower expression is detected.

Inbal et al., 1997, Nature 390:180-184, teach that lower expression of DAP exhibit highly aggressive metastatic behavior in murine lung cancer models.

The studies in Inbal et al., are done using murine lung cancer models. In other words, Inbal et al., do not teach DAP expression in human NSCLC tumors. However, Esteller et al., of record (1999, IDS, pages 67-70) teach a method of assessing NSCLC tumorigenesis at various stages including in early stage in human comprising assessing expression of the gene encoding DAP-kinase in lung cells of the human patients with

NSCLC. See the *Abstract* and *Materials and Methods* on page 67 and *Results* on page 68. The incidence of DAP-kinase promoter hypermethylation was observed in 5 of the 22 patients. See the Patient Numbers 1, 64, 84, 106 and 112, wherein patients 84 and 106 have an early stage, i.e., diagnostic stage I NSCLC tumor. See Table 1. In contrast, **none** of the 22 paired lung **normal** tissues exhibited abnormal promoter hypermethylation of any gene. See page 68, second column, the last sentence of the top paragraph. Esteller et al also state that silencing of tumor suppressor genes by promoter hypermethylation is a common feature in human cancer. Moreover, the loss of expression of the DAP kinase gene had been correlated with metastatic potential in experimental lung cancer models. On the basis of these observations, they examined 22 NSCLC patients to detect abnormal promoter hypermethylation in genes including DAP kinase in primary tumors. See the third paragraph at the second column on page 67.

Thus, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to arrive the claimed invention with a reasonable expectation of success, given Esteller et al teach all the necessary reagents for detection, and Inbal et al., teach aggressiveness of tumor when DAP expression is lost. One of ordinary skill would have been motivated to use more aggressive treatment for more aggressive tumor.

Claims 1, 45-48, 50-51 rejected under 35 U.S.C. 103(a) as being unpatentable over Inbal et al., 1997, Nature 390:180-184 in view of Esteller et al., of record (1999,

IDS, pages 67-70) as applied to claims 53, 54, 56, and 58-66 above, and further in view of Field et al. of record (IDS filed on Nov. 08, 2004).

The claims are drawn to a method of diagnosing non-small cell lung cancer (NSCLC) in a human, the method comprising assessing expression of the gene encoding DAP-kinase in lung cells of the human, whereby a lower degree of expression of the gene in the human relative to a normal level of expression of the gene in humans not afflicted with NSCLC is an indication that the human is afflicted with NSCLC, wherein the sample being used is a bronchial lavage.

See the teachings of Inbal et al., and Esteller et al., above.

Neither Inbal et al., nor Esteller et al., teach detection of DAP-kinase in bronchial lavage. However, Field et al., teach that DNA detection is possible in sample from bronchial lavage.

Thus, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to arrive at the claimed invention with a reasonable expectation of success because Field et al., teach bronchial lavage sample is being used for detection of early NSCLC markers.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MISOOK YU  
Primary Examiner  
Art Unit 1642

/Misook Yu/